REMARKS

Claim 1, as amended, and claims 2-5, 7-12, 41-43, and 55 are pending in the application. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

Applicants wish to thank Examiner Sajjadi and Examiner Woitach for meeting with Dr. John Lamerdin, Dr. Murielle Veniant-Ellison, and Applicants' undersigned representative on December 11, 2007 to discuss the instant application and for helpful discussions provided in the Interview that have materially advanced prosecution of this application. As requested by Examiner Sajjadi and Examiner Woitach during the Interview, Applicants hereby submit for consideration the enclosed Declaration of Dr. Murielle Veniant-Ellison under 37 C.F.R. § 1.132, which clearly establishes that the asserted utility for the claimed invention is specific, substantial, and credible. Applicants also wish to thank Examiner Sajjadi for his helpful discussions on December 27, 2007 regarding Dr. Veniant-Ellison's Declaration.

1. Objection to the claims

The Office Action contains an objection to claim 1 because the "4" in the phrase "either SEQ D NO: 2 or SEQ ID NO: 4" appears to have been deleted from the claim (by strikethrough) in error.

Applicants have amended claim 1to reintroduce the "4," which was deleted from the claim in error, and respectfully request that this objection be withdrawn.

2. Rejection of claims 1-5, 7-12, 41-43, and 55 under 35 U.S.C. §§ 101 and 112, first paragraph

The Office Action maintains a rejection of claims 1-5, 7-12, and 41-43 and asserts a rejection of claim 55 under 35 U.S.C. § 101 for reasons of record. In particular, the Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The Action also maintains a rejection of claims 1-5, 7-12, and 41-43 and asserts a rejection of claim 55 under 35 U.S.C. § 112, first paragraph, for reasons of record. In particular, the Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, and therefore, that one skilled in the art would not know how to

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use the claimed invention.

Applicants respectfully disagree with the Action's assertion that the instant application does not comply with the utility requirements of 35 U.S.C. §§ 101 and 112, first paragraph, and contend that the Declaration of Dr. David Ornitz under 37 C.F.R. § 1.132, submitted with Applicants' response to the Office Action mailed June 27, 2006, clearly establishes that the asserted utility for the claimed invention is specific, substantial, and credible. Nevertheless, in order to expedite prosecution of the pending claims to allowance, and in response to the Examiner's helpful comments provided in the December 11, 2007 Interview, Applicants have submitted the Declaration of Dr. Murielle Veniant-Ellison under 37 C.F.R. § 1.132 (Veniant-Ellison Declaration). Applicants contend that when the Declarations of Dr. Ornitz and Dr. Veniant-Ellison are taken together, there can be no doubt that the asserted utility for the claimed invention is specific, substantial, and credible, and therefore, that the instant application complies with the utility requirements of 35 U.S.C. §§ 101 and 112, first paragraph. Applicants, therefore, respectfully request that the rejections under 35 U.S.C. §§ 101 and 112, first paragraph be withdrawn.

With respect to Dr. Veniant-Ellison's Declaration, Applicants note that in the first portion of her Declaration, Dr. Veniant-Ellison discusses the results of Amgen's analysis of human and murine FGF-21, which indicates the potential effectiveness of FGF-21 polypeptides in the treatment of metabolic disorders such as diabetes and obesity (Veniant-Ellison Declaration, ¶¶ 3-10). In her Declaration, Dr. Veniant-Ellison relies on experimental results as originally set forth in the application as filed, and the results of experiments performed thereafter that are consistent with the results and disclosure of the application as filed.

Applicants also note that Dr. Veniant-Ellison states that she has reviewed Dr. Ornitz' Declaration and that she agrees with Dr. Ornitz' conclusions (Veniant-Ellison Declaration, ¶ 11).

Applicants further note that Dr. Veniant-Ellison states that she has reviewed U.S. Application No. 09/391,861 (the '861 application), and that based on her understanding of the '861 application, she believes that the '861 application provides support for the therapeutic use of FGF-21 (which is referred to as "FGF-like" in '861 application) for the treatment of metabolic diseases such as diabetes and obesity (Veniant-Ellison Declaration, ¶ 12).

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In support of this conclusion, Dr. Veniant-Ellison first points to the description in the '861 application that FGF-21 is expressed primarily in the liver with lower levels of expression in lung and fetal liver (Veniant-Ellison Declaration, ¶ 12(a); *see*, *e.g.*, '861 application, page 4, line 39 to page 5, line 1; page 80, lines 14-16; page 80, lines 2-5; and Figures 4A-4C). Noting that gene expression pattern is an important tool for drug discovery, and further, that the liver is one of the major organs involved in the regulation of metabolic parameters, including diabetes, Dr. Veniant-Ellison concludes that the expression pattern of FGF-21 is very indicative of its potential involvement in diabetes (*Id.*).

Dr. Veniant-Ellison next points to the description in the '861 application that transgenic mice overexpressing FGF-21 show, among other things, a reduction in body weight and a reduction in liver weight as a percent of body weight (Veniant-Ellison Declaration, ¶ 12(b); *see*, *e.g.*, '861 application, page 4, lines 22-26). With respect to this disclosure, Dr. Veniant-Ellison states that it is well known in the art that the accumulation of lipids in the liver is linked to insulin resistance and type 2 diabetes, and further, that this correlates with liver tissue mass, adiposity, and overall body weight (*Id.*). Dr. Veniant-Ellison also states that it is known in the art that fat accumulates in the liver when the rate of delivery of fatty acids to hepatocytes exceeds their metabolic processing capacity, and that disturbances in mitochondrial ß-oxidation can result in the accumulation of triglycerides in the liver (*Id.*). Dr. Veniant-Ellison further states that liver accumulation of fat in patients with type 2 diabetes or with insulin resistance syndrome is mainly related to increased lipolysis of adipose tissue, with an increased flux of free fatty acids to the liver that exceeds the liver's capacity to export very low density lipoproteins (*Id.*). Dr. Veniant-Ellison therefore concludes that the reduction of body weights and liver weights of the transgenic mice overexpressing FGF-21 disclosed in the '861 application is indicative of an improvement in fat distribution in the body (naturally occurring with age) and specifically, in the liver, explaining resistance to diabetes (*Id.*).

Dr. Veniant-Ellison next points to the description in the '861 application that FGF-21 polypeptides can be used therapeutically to treat diabetes or fat deposition in the treatment of obesity (Veniant-Ellison Declaration, ¶ 12(c); *see*, *e.g.*, '861 application, page 5, lines 15-16 and 27).

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Dr. Veniant-Ellison concludes that based on her seven years of experience in developing therapeutics for the treatment of metabolic disorders such as diabetes and obesity, as well as on the disclosure in the '861 application that FGF-21 is expressed primarily in the liver, transgenic mice overexpressing FGF-21 have reduced liver and body weights, and that FGF-21 molecules can be used therapeutically to treat diabetes and obesity, she would have understood that the FGF-21 molecules described in the '861 application would have therapeutic use in the treatment of diabetes or obesity (Veniant-Ellison Declaration, ¶ 13). Dr. Veniant-Ellison noted that her conclusion did not differ from that of Dr. Ornitz (*Id.*).

Finally, Dr. Veniant-Ellison states that her work with FGF-21 indicates that the FGF-21 molecules described in the '861 application in fact exhibit therapeutic potential for treating diabetes or obesity (Veniant-Ellison Declaration, ¶ 14).

Applicants contend that Dr. Veniant-Ellison's Declaration, which indicates that the '861 application contains specific and substantial assertions of utility, is sufficient to establish that the claimed invention has patentable utility since "evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true." M.P.E.P. § 2107.02(IV). Clearly, Dr. Veniant-Ellison is a person of ordinary skill in the relevant art, and is a reliable source concerning what would be credible to one of ordinary skill in the art at the time the instant application was filed. Moreover, as evidenced by her Declaration, Dr. Veniant-Ellison believes that based on the teachings in the specification and knowledge in the art at the time of the filing of the application, one of ordinary skill in the art would have expected that the new FGF disclosed in the '861 application would have therapeutic use for the treatment of metabolic diseases such as diabetes and obesity.

"If the asserted utility is credible (i.e., believable based on the record or the nature of the invention), a rejection based on 'lack of utility' is not appropriate." M.P.E.P. § 2107.02(III)(A). Because Dr. Veniant-Ellison's Declaration establishes that "the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a 'specific and substantial utility') and the assertion would be considered credible by a person of ordinary skill in the art," M.P.E.P. § 2107(II), Applicants contend that the claimed invention is supported by an assertion of a specific and substantial utility that is credible, and therefore, respectfully request that the rejection

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under 35 U.S.C. § 101 be withdrawn.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

Applicants remind the Examiner of U.S. Patent No. 6,716,626, which issued on April 6, 2004 from U.S. Application No. 09/715,805 (the '805 application), filed November 16, 2000, and which claims the benefit of U.S. Provisional Application Nos. 60/203,633, filed May 11, 2000, and 60/166,540, filed November 18, 1999. In addition, Applicants would like to draw the Examiner's attention to U.S. Patent No. 7,259,248, which issued August 21, 2007 from U.S. Application No. 10/060,765, filed January 1, 2002; U.S. Application No. 11/405,24, which was filed on April 17, 2006, and which was published as U.S. Patent Application Publication No. US 2007/0238657 A1 on October 11, 2007; and U.S. Application No. 11/441,666, which was filed on May 26, 2006, and which was published as U.S. Patent Application Publication No. US 2007/0128619 A1 on June 6, 2007, each of which claims the benefit of the '805 application. Applicants further remind the Examiner that they have an earlier filing date and believe that they are the first and sole inventors of the claimed subject matter, and therefore, expect the Examiner to declare an interference if the pending claims are found to be allowable.

If Examiner Sajjadi believes it to be helpful, he is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,
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